10/070,277

L2: Entry 1 of 9 File: PGPB Jun 10, 2004

DOCUMENT-IDENTIFIER: US 20040111769 A1
TITLE: Sugar beet genes involved in stress tolerance

CLAIMS:

8. A method for enhancing stress tolerance in a plant comprising the expression or altering the expression of a nucleic acid encoding a dihydroorotase in cells, tissues or parts of said plant.

9. A method according to claim 8 wherein said nucleic acid encodes a dihydroorotase as defined in claim 4, or a homologue, an orthologue or a paralogue thereof.

# Hit List

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

**Search Results** - Record(s) 1 through 9 of 9 returned.

☐ 1. Document ID: US 20040111769 A1

**Using default format because multiple data bases are involved.**

L2: Entry 1 of 9 File: PGPB Jun 10, 2004

PGPUB-DOCUMENT-NUMBER: 20040111769
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040111769 A1

TITLE: Sugar beet genes involved in stress tolerance

PUBLICATION-DATE: June 10, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Kanhonou, Arthur Rodolphe | Valencia | | ES | |
| Serrano Salom, Ramon | Valencia | | ES | |
| Ros Palau, Roc | Valencia | | ES | |

US-CL-CURRENT: 800/289; 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 20030049686 A1

L2: Entry 2 of 9 File: PGPB Mar 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030049686
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030049686 A1

TITLE: Method for manufacturing mutnat library of proteins with various sizes and sequences

PUBLICATION-DATE: March 13, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Kim, Hak-Sung | Taejon | | KR | |
| Kim, Geun-Joong | Suwon | | KR | |
| Cheon, Young-Hoon | Taejon | | KR | |
| Lee, Dong-Eun | Taejon | | KR | |

US-CL-CURRENT: 435/7.1; 435/252.3, 435/69.1, 435/91.2, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

---

☐ 3. Document ID: US 20020102583 A1

L2: Entry 3 of 9 File: PGPB Aug 1, 2002

PGPUB-DOCUMENT-NUMBER: 20020102583
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020102583 A1

TITLE: Method for isolation of extrachromosomal amplified genes

PUBLICATION-DATE: August 1, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Wahl, Geoffrey M. | San Diego | CA | US | |
| Shimizu, Noriaki | San Diego | CA | US | |

US-CL-CURRENT: 435/6; 435/91.1, 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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☐ 4. Document ID: US 6537758 B2

L2: Entry 4 of 9 File: USPT Mar 25, 2003

US-PAT-NO: 6537758
DOCUMENT-IDENTIFIER: US 6537758 B2

TITLE: Method for isolating nucleic acid from micronuclei separated from a cell

DATE-ISSUED: March 25, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Wahl; Geoffrey M. | San Diego | CA | | |
| Shimizu; Noriaki | San Diego | CA | | |

US-CL-CURRENT: 435/6; 536/25.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

---

☐ 5. Document ID: US 6312908 B1

L2: Entry 5 of 9 File: USPT Nov 6, 2001

US-PAT-NO: 6312908
DOCUMENT-IDENTIFIER: US 6312908 B1

TITLE: Method for isolation of extrachromosomal amplified genes

DATE-ISSUED: November 6, 2001

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Wahl; Geoffrey M. | San Diego | CA | | |
| Shimizu; Noriaki | San Diego | CA | | |

US-CL-CURRENT: 435/6; 435/91.1, 435/91.2, 536/25.4, 536/25.41

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

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☐ 6. Document ID: US 6033849 A

L2: Entry 6 of 9 File: USPT Mar 7, 2000

US-PAT-NO: 6033849
DOCUMENT-IDENTIFIER: US 6033849 A

TITLE: Method for isolation of extrachromosomal amplified genes

DATE-ISSUED: March 7, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Wahl; Geoffrey M. | San Diego | CA | | |
| Shimizu; Noriaki | San Diego | CA | | |

US-CL-CURRENT: 435/6; 435/91.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

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☐ 7. Document ID: US 5981182 A

L2: Entry 7 of 9 File: USPT Nov 9, 1999

US-PAT-NO: 5981182
DOCUMENT-IDENTIFIER: US 5981182 A

TITLE: Vector constructs for the selection and identification of open reading frames

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|

| | | |
|---|---|---|
| Jacobs, Jr.; William R. | City Island | NY |
| Daugelat; Sabine | Bronx | NY |

US-CL-CURRENT: 435/6; 435/320.1, 435/69.1, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

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☐ 8. Document ID: US 5968502 A

L2: Entry 8 of 9 File: USPT Oct 19, 1999

US-PAT-NO: 5968502
DOCUMENT-IDENTIFIER: US 5968502 A

TITLE: Protein production and protein delivery

DATE-ISSUED: October 19, 1999

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Treco; Douglas | Arlington | MA | | |
| Heartlein; Michael W. | Boxborough | MA | | |
| Selden; Richard F | Wellesley | MA | | |

US-CL-CURRENT: 424/93.21; 424/425, 435/320.1, 435/325, 435/455, 435/69.1, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

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☐ 9. Document ID: US 5213972 A

L2: Entry 9 of 9 File: USPT May 25, 1993

US-PAT-NO: 5213972
DOCUMENT-IDENTIFIER: US 5213972 A

TITLE: Fermentation process for the production of pyrimidine deoxyribonucleosides

DATE-ISSUED: May 25, 1993

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| McCandliss; Russell J. | Gaithersburg | MD | | |
| Anderson; David M. | Rockville | MD | | |

US-CL-CURRENT: 435/89; 435/252.3, 435/252.33, 435/320.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw De

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Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

| Terms | Documents |
|---|---|
| dihydroorotase.clm. | 9 |

**Display Format:** - Change Format

Previous Page Next Page Go to Doc#

L2: Entry 3 of 22 File: PGPB Sep 4, 2003

DOCUMENT-IDENTIFIER: US 20030166615 A1
TITLE: Protein kinase and phosphatase inhibitors and methods for designing them

Detail Description Paragraph:
[0077] The next class of M.sub.1 functionality which was explored was the boronic acid group. This functional group is an intriguing candidate for M.sub.1 for a number of reasons: 1) It can exist in a non-ionic state so that it should not prevent passive absorption of non-peptide inhibitors across cell membranes. 2) The planar, trigonal, boron acids might form reversible tetrahedral covalent borate complexes (a well known property of boronic acids, see Loomis & Durst, 1992) through their vacant 2p orbitals with anions present in the protein kinase active site, such as the catalytic Asp carboxyl group, or the ATP/ADP terminal phosphate oxygens. This ability to form borate complexes with active site nucleophiles has been extensively utilized to develop slow binding inhibitors of serine proteases (e.g. see Kettner & Shenvi, 1984), wherein the nucleophilic serine OH forms a covalent bond with the vacant 2p orbital in the boronic acid resulting in a tetrahedral borate complex (e.g. see Skordalakes et al., 1997). Also, an intramolecular complex of a boronic acid with a urea NH.sub.2 was used to prepare transition state analogs inhibitors of dihydroorotase (Kinder et al., 1990). 3) Boronic acids act as Lewis acids and are converted to tetrahedral hydrates in water by forming borate complexes with water or hydroxide ions. Therefore, it is also possible that these boronic acid hydrates may function as phosphate mimics and M.sub.1 modules as proposed in FIG. 2. This hydration property was utilized by Baggio et al. (1997) wherein a hydrated boronic acid functioned as a transition state analog inhibitor functionality for arginase. These researchers evaluated the inhibited complex by x-ray and showed that the hydrated boronic acid functionality formed two hydrogen bonds with the active site catalytic Glu-277 carboxyl side chain and one of the other hydrated boronic acid OH's interacted with two catalytic Mn.sup.2+'s in the active site. These binding interactions are closely analogous to those proposed in protein kinase active sites, i.e. H-bonds to the catalytic Asp side chain carboxyl group and interactions with the active site Mg.sup.2+'s (see FIGS. 2 and 4). The use of boronic acids for protein kinase inhibitors has not been explored previously.

# Hit List

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

**Search Results** - Record(s) 1 through 10 of 22 returned.

☐ 1. Document ID: US 20040191783 A1

**Using default format because multiple data bases are involved.**

L2: Entry 1 of 22 File: PGPB Sep 30, 2004

PGPUB-DOCUMENT-NUMBER: 20040191783
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040191783 A1

TITLE: Low density micro-array analysis in human breast cancer

PUBLICATION-DATE: September 30, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Leclercq, Guy | Bruxelles | | BE | |
| Remacle, Jose | Malonne | | BE | |
| Lacroix, Marc | Baelen | | BE | |
| Zammatteo, Nathalie | Gelbressee | | BE | |
| de Longueville, Francoise | Natoye | | BE | |

US-CL-CURRENT: 435/6; 435/287.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 2. Document ID: US 20040033596 A1

L2: Entry 2 of 22 File: PGPB Feb 19, 2004

PGPUB-DOCUMENT-NUMBER: 20040033596
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040033596 A1

TITLE: In vitro mutagenesis, phenotyping, and gene mapping

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Threadgill, David W. | Chapel Hill | NC | US | |
| Lee, Daekee | Chapel Hill | NC | US | |

US-CL-CURRENT: 435/325; 435/366, 435/419

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 3. Document ID: US 20030166615 A1

L2: Entry 3 of 22 File: PGPB Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030166615
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030166615 A1

TITLE: Protein kinase and phosphatase inhibitors and methods for designing them

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Hangauer, David G. JR. | Amherst | NY | US | |
| El-Araby, Moustafa E. | Plainsboro | NJ | US | |
| Milkiewicz, Karen L. | Exton | PA | US | |

US-CL-CURRENT: 514/80; 514/233.5, 514/254.09, 514/307, 514/419, 544/143, 544/373, 546/146, 546/23, 548/414, 548/494

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 4. Document ID: US 20030166201 A1

L2: Entry 4 of 22 File: PGPB Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030166201
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030166201 A1

TITLE: Selection systems for genetically modified cells

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Jensen, Michael C. | Pasadena | CA | US | |

US-CL-CURRENT: 435/191; 435/320.1, 435/325, 435/69.1, 514/44, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 5. Document ID: US 20030148311 A1

L2: Entry 5 of 22 File: PGPB Aug 7, 2003

PGPUB-DOCUMENT-NUMBER: 20030148311
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030148311 A1

TITLE: Aspartate carbamyltransferase as herbicidal target

PUBLICATION-DATE: August 7, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Ehrhardt, Thomas | Speyer | | DE | |
| Lerchl, Jens | Ladenburg | | DE | |
| Nigel, Marc Stitt | Edingen-Neckarhausen | | DE | |
| Zrenner, Rita | Ladenburg | | DE | |
| Ritter, Tina Maria | Dilsberg | | DE | |

US-CL-CURRENT: 435/6; 435/15, 435/193

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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☐ 6. Document ID: US 20020058244 A1

L2: Entry 6 of 22 File: PGPB May 16, 2002

PGPUB-DOCUMENT-NUMBER: 20020058244
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020058244 A1

TITLE: Method for detecting uracil biosynthesis inhibitors and their use as herbicides

PUBLICATION-DATE: May 16, 2002

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|---|---|---|---|---|
| Pedersen, Marianne K. | Princeton Junction | NJ | US | |
| Birk, Iwona T. | Raleigh | NC | US | |
| Orth, Ann B. | Langhorne | PA | US | |
| Singh, Bijay K. | Apex | NC | US | |
| Tecle, Berhane | Lawrenceville | NJ | US | |
| Kameswaran, Venkataraman | Pennington | NJ | US | |
| Szucs, Stephen S. | Lawrenceville | NJ | US | |

US-CL-CURRENT: 435/4; 504/116.1, 504/282, 548/370.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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☐ 7. Document ID: US 6825169 B1

L2: Entry 7 of 22 File: USPT Nov 30, 2004

US-PAT-NO: 6825169
DOCUMENT-IDENTIFIER: US 6825169 B1

TITLE: Inhibitors of dipeptidyl-aminopeptidase type IV

DATE-ISSUED: November 30, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Bachovchin; William W. | Melrose | MA | | |
| Plaut; Andrew G. | Boston | MA | | |
| Flentke; George R. | Boston | MA | | |

US-CL-CURRENT: 514/19; 514/15, 514/16, 514/17, 514/18, 530/327, 530/328, 530/329, 530/330, 530/331, 568/1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. De

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☐ 8. Document ID: US 6770628 B2

L2: Entry 8 of 22 File: USPT Aug 3, 2004

US-PAT-NO: 6770628
DOCUMENT-IDENTIFIER: US 6770628 B2
** See image for Certificate of Correction **

TITLE: Hematopoietic stimulation

DATE-ISSUED: August 3, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Wallner; Barbara P. | Weston | MA | | |
| Jones; Barry | Cambridge | MA | | |
| Miller; Glenn T. | Haverhill | MA | | |
| Adams; Sharlene | Watertown | MA | | |

US-CL-CURRENT: 514/19; 514/13, 514/14, 514/15, 514/16, 514/17, 514/18, 514/423

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. De

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☐ 9. Document ID: US 6703238 B2

L2: Entry 9 of 22 File: USPT Mar 9, 2004

US-PAT-NO: 6703238
DOCUMENT-IDENTIFIER: US 6703238 B2

TITLE: Methods for expanding antigen-specific T cells

DATE-ISSUED: March 9, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Bachovchin; William | Melrose | MA | | |
| Wallner; Barbara | Weston | MA | | |

US-CL-CURRENT: 435/325; 424/184.1, 424/195.11, 435/377, 435/383, 514/2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

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☐ 10. Document ID: US 6692753 B2

L2: Entry 10 of 22 File: USPT Feb 17, 2004

US-PAT-NO: 6692753
DOCUMENT-IDENTIFIER: US 6692753 B2

TITLE: Potentiation of the immune response

DATE-ISSUED: February 17, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---|---|---|---|---|
| Huber; Brigitte T. | Boston | MA | | |
| Schmitz; Tracy | Cambridge | MA | | |
| Underwood; Robert | Quincy | MA | | |

US-CL-CURRENT: 424/278.1; 514/18, 514/2, 514/408

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

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Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

| Terms | Documents |
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| dihydroorotase same inhibitor? | 22 |

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**Display Format:** - Change Format

Previous Page Next Page Go to Doc#

# WEST Search History

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DATE: Wednesday, February 16, 2005

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| ☐ | L3 | dihydroorotase same inhibitor?.clm. | 0 |
| ☐ | L2 | dihydroorotase same inhibitor? | 22 |
| ☐ | L1 | dihydroorotase and inhibitor? | 322 |

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# WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Wednesday, February 16, 2005

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| ☐ | L12 | L11 and (potato? or solanum) | 0 |
| ☐ | L11 | dihydrooratase and dna | 22 |
| ☐ | L10 | dihydrooratase same dna | 1 |
| ☐ | L9 | dihydrooratase with dna | 0 |
| ☐ | L8 | dihydrooratase with solanum | 0 |
| ☐ | L7 | dihydrooratase same solanum | 0 |
| ☐ | L6 | solanum | 5249 |
| ☐ | L5 | L3 and solanum | 0 |
| ☐ | L4 | L3 and potatoes | 0 |
| ☐ | L3 | dihydrooratase | 25 |
| ☐ | L2 | dihydrooratase and solanum | 0 |
| ☐ | L1 | dihydrooratase.clm. | 2 |

END OF SEARCH HISTORY

# WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Wednesday, February 16, 2005

| Hide? | Set Name | Query | Hit Count |
|---|---|---|---|
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| ☐ | L5 | dihydroorotase same solanum | 0 |
| ☐ | L4 | dihydroorotase with solanum | 0 |
| ☐ | L3 | dihydroorotase and solanum | 15 |
| ☐ | L2 | dihydroorotase.clm. | 9 |
| ☐ | L1 | dihydroorotase same solanum | 0 |

END OF SEARCH HISTORY

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.42       0.42

FILE 'MEDLINE' ENTERED AT 11:25:02 ON 16 FEB 2005

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=> s  Inhibitor? and Dihydroorotase
L1          273 INHIBITOR? AND DIHYDROOROTASE

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2          146 DUP REM L1 (127 DUPLICATES REMOVED)

=> s l2 and (plant? or solanum or arbidopsis or tobacco or wheat)
L3            3 L2 AND (PLANT? OR SOLANUM OR ARBIDOPSIS OR TOBACCO OR WHEAT)

=> d l3 1-3 ibib ab

L3   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2000:592846  HCAPLUS
DOCUMENT NUMBER:          133:173007
TITLE:                    Non-targeted activation of endogenous gene expression
                          or over-expression by recombination methods in situ
INVENTOR(S):              Harrington, John J.; Sherf, Bruce; Rundlett, Stephen
PATENT ASSIGNEE(S):       Athersys, Inc., USA
SOURCE:                   PCT Int. Appl., 241 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2000049162         A2    20000824    WO 2000-US4429          20000222
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             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
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         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 6602686            B1    20030805    US 1999-455659          19991207
     US 6410266            B1    20020625    US 2000-479122          20000107
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| | | | | |
|---|---|---|---|---|
| US 6670185 | B1 | 20031230 | US 2000-479123 | 20000107 |
| US 6361972 | B1 | 20020326 | US 2000-481375 | 20000110 |
| US 6541221 | B1 | 20030401 | US 2000-481282 | 20000111 |
| US 6524824 | B1 | 20030225 | US 2000-481355 | 20000112 |
| US 6524818 | B1 | 20030225 | US 2000-484997 | 20000118 |
| US 6623958 | B1 | 20030923 | US 2000-484996 | 20000118 |
| US 6740503 | B1 | 20040525 | US 2000-484317 | 20000118 |
| CA 2364267 | AA | 20000824 | CA 2000-2364267 | 20000222 |
| EP 1155131 | A2 | 20011121 | EP 2000-908750 | 20000222 |
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| BR 2000008313 | A | 20030923 | BR 2000-8313 | 20000222 |
| JP 2004501601 | T2 | 20040122 | JP 2000-599886 | 20000222 |
| US 2004162416 | A1 | 20040819 | US 2001-760897 | 20010117 |
| ZA 2001006777 | A | 20030514 | ZA 2001-6777 | 20010816 |
| US 2003180267 | A1 | 20030925 | US 2002-331329 | 20021230 |
| PRIORITY APPLN. INFO.: | | | US 1999-253022 | A 19990219 |
| | | | US 1999-263814 | A 19990308 |
| | | | US 1999-276820 | A 19990326 |
| | | | US 1997-941223 | B2 19970926 |
| | | | US 1998-159643 | B2 19980924 |
| | | | WO 2000-US4429 | W 20000222 |
| | | | US 2000-515124 | B1 20000227 |

AB The present invention is directed generally to activating gene expression or causing over-expression of a gene by recombination methods in situ. The invention also is directed generally to methods for expressing an endogenous gene in a cell at levels higher than those normally found in the cell. In one embodiment of the invention, expression of an endogenous gene is activated or increased following integration into the cell, by non-homologous or illegitimate recombination, of a regulatory sequence that activates expression of the gene. In another embodiment, the expression of the endogenous gene may be further increased by co-integration of one or more amplifiable markers, and selecting for increased copies of the one or more amplifiable markers located on the integrated vector. In another embodiment, the invention is directed to activation of endogenous genes by non-targeted integration of specialized activation vectors, which are provided by the invention, into the genome of a host cell. The invention also provides methods for the identification, activation, isolation, and/or expression of genes undiscoverable by current methods since no target sequence is necessary for integration. The invention also provides methods for isolation of nucleic acid mols. (particularly cDNA mols.) encoding a variety of proteins, including transmembrane proteins, and for isolation of cells expressing such transmembrane proteins which may be heterologous transmembrane proteins. The invention also is directed to isolated genes, gene products, nucleic acid mols., to compns. comprising such genes, gene products and nucleic acid mols., and to vectors and host cells comprising such genes and nucleic acid mols., that may be used in a variety of therapeutic and diagnostic applications. Thus, by the present invention, endogenous genes, including those assocd. with human disease and development, may be activated and isolated without prior knowledge of the sequence, structure, function, or expression profile of the genes.

L3 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:748948 HCAPLUS

DOCUMENT NUMBER: 128:150233

TITLE: The complete genome sequence of the gram-positive bacterium Bacillus subtilis

AUTHOR(S): Kunst, F.; Ogasawara, N.; Moszer, I.; Albertini, A. M.; Alloni, G.; Azevedo, V.; Bertero, M. G.; Bessieres, P.; Bolotin, A.; Borchert, S.; Borriss, R.; Boursier, L.; Brans, A.; Braun, M.; Brignell, S. C.; Bron, S.; Brouillet, S.; Bruschi, C. V.; Caldwell, B.; Capuano, V.; Carter, N. M.; Choi, S.-K.; Codani, J.-J.; Connerton, I. F.; Cummings, N. J.; Daniel, R.

A.; Denizot, F.; Devine, K. M.; Dusterhoft, A.; Ehrlich, S. D.; Emmerson, P. T.; Entian, K. D.; Errington, J.; Fabret, C.; Ferrari, E.; Foulger, D.; Fritz, C.; Fujita, M.; Fujita, Y.; Fuma, S.; Galizzi, A.; Galleron, N.; Ghim, S.-Y.; Glaser, P.; Goffeau, A.; Golightly, E. J.; Grandi, G.; Guiseppi, G.; Guy, B. J.; Haga, K.; et al.

CORPORATE SOURCE: Unite de Biochemie Microbienne, Inst. Pasteur, Paris, 75724, Fr.

SOURCE: Nature (London) (1997), 390(6657), 249-256
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacillus subtilis is the best-characterized member of the gram-pos. bacteria. Its genome of 4,214,810 base pairs comprises 4100 protein-coding genes. Of these protein-coding genes, 53% are represented once, while a quarter of the genome corresponds to several gene families that have been greatly expanded by gene duplication, the largest family contg. 77 putative ATP-binding transport proteins. In addn., a large proportion of the genetic capacity is devoted to the utilization of a variety of carbon sources, including many **plant**-derived mols. The identification of 5 signal peptidase genes, as well as several genes for components of the secretion app., is important given the capacity of Bacillus strains to secrete large amts. of industrially important enzymes. Many of the genes are involved in the synthesis of secondary metabolites, including antibiotics, that are more typically assocd. with Streptomyces species. The genome contains .gtoreq.10 prophages or remnants of prophages, indicating that bacteriophage infection has played an important evolutionary role in horizontal gene transfer, in particular in the propagation of bacterial pathogenesis.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 3 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN

ACCESSION NUMBER: 2001-08527 BIOTECHDS

TITLE: New DNA encoding **plant dihydroorotase**, for producing herbicide-resistant **plants** and for screening for compounds that can inhibit **dihydroorotase** and that can be used as herbicides; **tobacco** and Arabidopsis thaliana transgenic **plant** construction

AUTHOR: Ehrhardt T; Lerchl J; Stitt N M; Zrenner R; Schroeder M
PATENT ASSIGNEE: BASF
LOCATION: Ludwigshafen, Germany.

PATENT INFO: WO 2001018190 15 Mar 2001
APPLICATION INFO: WO 2000-EP8581 2 Sep 2000
PRIORITY INFO: DE 1999-1042742 7 Sep 1999
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 2001-235198 [24]

AB A DNA sequence (I) containing the coding region for a **plant dihydroorotase** (DHO, EC-3.5.2.3) with a DNA sequence (S1) of 1,271 bp is claimed. Also claimed are: a DNA sequence that hybridizes to (S1) and encodes a protein with DHO activity; a protein containing 100 amino acids from a 346 residue protein sequence; identifying substances that inhibit activity of DHO or act as herbicides by inhibition of DHO; and a test system based on expression of (S1) for identifying herbicidal **inhibitors** of DHA. In an example, a cDNA bank from potato was constructed in plasmid pBS-SK and tested in for complementation of the defect in Escherichia coli CGSC5152 which lacks the DHO gene. The longest clone was sequenced (S1) which included a 1,049 bp open reading frame that encodes DHO. The gene was expressed in vector/host system as a fusion protein or introduced into **plant** transformation vectors. A sequence of 1,962 bp was isolated from **tobacco**

(Nicotiana tabacum) cDNA bank by using a DNA probes encoding DHO in Arabidopsis thaliana. The above can be used to produce DHO and to produce **plants** with increased resistance to DHO-inactivating herbicides. (38pp)

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=> d his

     (FILE 'HOME' ENTERED AT 11:24:00 ON 16 FEB 2005)

     FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT
     11:25:02 ON 16 FEB 2005
L1           273 S  INHIBITOR? AND DIHYDROOROTASE
L2           146 DUP REM L1 (127 DUPLICATES REMOVED)
L3             3 S L2 AND (PLANT? OR SOLANUM OR ARBIDOPSIS OR TOBACCO OR WHEAT)

=> s l2 and 1980-1999/py
   4 FILES SEARCHED...
L4           78 L2 AND 1980-1999/PY

=> focus l4
PROCESSING COMPLETED FOR L4
L5            78 FOCUS L4 1-

=> d l5 1-10 ibib ab

L5   ANSWER 1 OF 78  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1994:557742  HCAPLUS
DOCUMENT NUMBER:          121:157742
TITLE:                    Synthesis of a phosphinic acid transition state analog
                          inhibitor of dihydroorotase
AUTHOR(S):                Cao, Yu; Christopherson, Richard I.; Elix, John A.;
                          Gaul, Kim L.
CORPORATE SOURCE:         Chem. Dep., Aust. Natl. Univ., Canberra, 0200,
                          Australia
SOURCE:                   Australian Journal of Chemistry (1994),
                          47(5), 903-11
                          CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
OTHER SOURCE(S):          CASREACT 121:157742
AB   The synthesis of the phosphinic acid 4-hydroxy-6-oxo-1,4-azaphosphinane-2-
     carboxylic acid 4-oxide (11, shown as I) is described.  The phosphinic
     acid I was designed as a transition state analog inhibitor of
     dihydroorotase.  Thus, treating MeO2CCH2P(OEt)2 with BzOH and then
     with CF3CONHC(:CH2)CO2Me gave 74% MeO2CCH2P(O)(OEt)CH2CH(CO2Me)NHCOCF3,
     which when treated with concd. HCl gave 77% HO2CCH2P(O)(OH)CH2CH(NH2)CO2H.
     Cyclization of the latter compd. with EDC gave 21% I.

L5   ANSWER 2 OF 78  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1993:113643  HCAPLUS
DOCUMENT NUMBER:          118:113643
TITLE:                    A crystallographic and molecular mechanics study of
                          inhibitors of dihydroorotase
AUTHOR(S):                Hambley, Trevor W.; Phillips, Leonidas; Poiner,
                          Anthony C.; Christopherson, Richard I.
CORPORATE SOURCE:         Dep. Inorg. Chem., Univ. Sydney, 2006, Australia
SOURCE:                   Acta Crystallographica, Section B:  Structural Science
                          (1993), B49(1), 130-6
                          CODEN: ASBSDK; ISSN: 0108-7681
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Me L-dihydroorotate is orthorhombic, space group P212121, with a 6.941(2),
     b 9.708(2), c 23.329(5) .ANG., Z = 8, dc = 1.455, T = 294 K, final R =
     0.036 for 793 reflections.  Me L-6-thiodihydroorotate is monoclinic, space
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group P21, with a 6.235(2), b 20.821(4), c 6.882(1) .ANG., .beta. 110.82(2).degree., Z = 4, dc = 1.497, 392, T = 294 K, final R = 0.037 for 1404 reflections. Di-Me trans-2-oxohexahydropyrimidine-4,6-dicarboxylate is triclinic, space group P.hivin.1, with a 7.3977(5), b 8.4149(8), c 9.314(1) .ANG., .alpha. 74.65(1), .beta. 68.08(1), .gamma. 98.77(1).degree., Z = 2, dc = 1.428, 294 K, final R = 0.040 for 1468 reflections. Di-Me 2-oxo-1,2,3,6-tetrahydropyrimidine-4,6-dicarboxylate is triclinic, space group P.hivin.1, with a 7.481(3), b 8.344(3), c 9.042(5) .ANG., .alpha. 95.05(3), .beta. 111.02(3), .gamma. 108.31(3).degree., Z = 2, dc = 1.460, T = 294 K, final R = 0.040 for 1253 reflections. The 3-dimensional structures of the Me esters of dihydroorotate and 3 potential **inhibitors** of the enzyme, **dihydroorotase**, were detd. At. coordinates are given. Correlations between the structures of these compds. and their **inhibitory** activities are discussed. It is postulated that for strong binding to **dihydroorotase** to occur, a pyrimidine ring with 3 groups capable of forming strong interactions is required; 2 of these groups must be coplanar with the ring or equatorially disposed, and the 3rd group must be axially disposed. Mol. mechanics modeling was used to study the conformational isomerism of the compds. and the role it plays in detg. binding and consequent inhibition of **dihydroorotase**.

L5 ANSWER 3 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:406545 HCAPLUS
DOCUMENT NUMBER: 109:6545
TITLE: Preparation and testing of 2-oxo-4-carboxypyrimidines as neoplasm **inhibitors** and antimalarials
INVENTOR(S): Schmalzl, Karl John; Sharma, Suresh Chandra; Christopherson, Richard Ian
PATENT ASSIGNEE(S): University of Melbourne, Australia; University of Sydney
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE | |
|---|---|---|---|---|---|---|
| EP 260057 | A2 | 19880316 | EP 1987-307744 | | 19870902 | <-- |
| EP 260057 | A3 | 19890201 | | | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | | | |
| AU 8777692 | A1 | 19880331 | AU 1987-77692 | | 19860902 | <-- |
| AU 595062 | B2 | 19900322 | | | | |
| JP 63119471 | A2 | 19880524 | JP 1987-220095 | | 19870901 | <-- |
| US 4873228 | A | 19891010 | US 1987-91761 | | 19870901 | <-- |
| ZA 8706552 | A | 19880525 | ZA 1987-6552 | | 19870902 | <-- |
| PRIORITY APPLN. INFO.: | | | AU 1986-7811 | A | 19860902 | |
| | | | AU 1986-8161 | A | 19860922 | |

OTHER SOURCE(S): MARPAT 109:6545
AB The title compds. [I; R1, R2 = OH, peptide residue, alkoxy, alkoxymethyl, amino, any group able to be hydrolyzed in vivo to OH; R3, R4 = H, alkyl, hydroxyalkyl, tetrahydrofuranyl, tetrahydropyranyl, (acetylated) sugar residue, any group hydrolyzable in vitro to H; R5 = H, halo, alkyl; R6 = alkyl, 1-methyl-4-nitroimidazol-5-yl; A = H, B = COR2; AB = S] were prepd. as **inhibitors** of **dihydroorotase**. Di-Me 2-hydroxypyrimidine-4,6-dicarboxylate (prepn. given) was reduced with Zn/HOAc to give 28% di-Me 2-oxo-1,2,3,6-tetrahydropyrimidine-4,6-dicarboxylate, which was refluxed 30 min in 1M NaOH to give 50% 2-oxo-1,2,3,6-tetrahydropyrimidine-4,6-dicarboxylic acid (HDDP). HDDP bound **dihydroorotase** with a Ki of 0.48 .mu.m.

L5 ANSWER 4 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:419878 HCAPLUS

DOCUMENT NUMBER: 113:19878
TITLE: Pyrimidine biosynthesis in parasitic protozoa: purification of a monofunctional **dihydroorotase** from Plasmodium berghei and Crithidia fasciculata
AUTHOR(S): Krungkrai, Jerapan; Cerami, Anthony; Henderson, Graeme B.
CORPORATE SOURCE: Lab. Med. Biochem., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Biochemistry (**1990**), 29(26), 6270-5
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Dihydroorotase** (DHOase) was purified from 2 parasitic protozoa, C. fasciculata (.apprx.16,000-fold) and P. berghei (.apprx.790-fold). The C. fasciculata enzyme had a native mol. wt. (Mr) of 42,000, detd. by gel filtration chromatog., and showed a single detectable protein band on SDS-PAGE with a Mr of 44,000. The DHOase from P. berghei had a native Mr of 40,000 and a subunit Mr on SDS-PAGE of 38,000. The DHOase from both parasites, in contrast to the mammalian enzyme which residues on a trifunctional protein of the 1st 2 enzymes of the pyrimidine biosynthesis pathway, carbamoylphosphate synthase and aspartate transcarbamylase, is a monomeric enzyme and has no oligomeric structure as studied by chem. crosslinking with di-Me suberimidate. The rate of cyclization of N-carbamoyl-L-aspartate (L-CA) by the C. fasciculata enzyme was relatively high at acidic pH, decreasing to a very low rate at alk. pH. In contrast, the rate of ring cleavage of L-5,6-dihydroorotate (L-DHO) was very low at acidic pH and increased to higher rate at alk. pH. These pH-activity profiles gave an intersection at pH 6.6. The Km and kcat for L-CA were 0.846 mM and 39.2 min-1, resp.; for L-DHO, they were 25.85 .mu.M and 258.6 min-1. The cryoprotectant DMSO used as stabilizing agent in the complete purifn. and storage, markedly affected the DHOase activity. DMSO increased the catalytic efficiency of the enzyme, as measured by kcat/Km, in the ring cyclization reaction but had no effect on the ring cleavage reaction. In spite of their marked phys. differences, kinetic and **inhibitor** studies with 5-substituted derivs. of orotic acid suggest that the protozoan, mammalian, and prokaryotic enzymes have a common catalytic mechanism.

L5 ANSWER 5 OF 78 MEDLINE on STN
ACCESSION NUMBER: 89229035 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2565732
TITLE: Mercaptan and dicarboxylate **inhibitors** of hamster **dihydroorotase**.
AUTHOR: Christopherson R I; Schmalzl K J; Szabados E; Goodridge R J; Harsanyi M C; Sant M E; Algar E M; Anderson J E; Armstrong A; Sharma S C; +
CORPORATE SOURCE: Department of Biochemistry, University of Sydney, New South Wales, Australia.
SOURCE: Biochemistry, **(1989 Jan 24)** 28 (2) 463-70.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 20000303
Entered Medline: 19890622

AB In mammals, **dihydroorotase** is part of a trifunctional protein, dihydroorotate synthetase, which catalyzes the first three reactions of de novo pyrimidine biosynthesis. **Dihydroorotase** catalyzes the formation of a peptide-like bond between the terminal ureido nitrogen and the beta-carboxyl group of N-carbamyl-L-aspartate to yield heterocyclic L-dihydroorotate. A variety of evidence suggests that

**dihydroorotase** may have a catalytic mechanism similar to that of a zinc protease [Christopherson, R. I., & Jones, M. E. (1980) J. Biol. Chem. 255, 3358-3370]. Tight-binding **inhibitors** of the zinc proteases, carboxypeptidase A, thermolysin, and angiotensin-converting enzyme have been synthesized that combine structural features of the substrates with a thiol or carboxyl group in an appropriate position to coordinate a zinc atom bound at the catalytic site. We have synthesized (4R)-2-oxo-6-thioxohexahydropyrimidine-4-carboxylate (L-6-thiodihydroorotate) and have found that this analogue is a potent competitive **inhibitor** of **dihydroorotase** with a dissociation constant (Ki) in the presence of excess Zn2+ ion of 0.17 +/- 0.02 microM at pH 7.4. The potency of inhibition by L-6-thiodihydroorotate in the presence of divalent metal ions decreases in the order Zn2+ greater than Ca2+ greater than Co2+ greater than Mn2+ greater than Ni2+; L-6-thiodihydroorotate alone is less **inhibitory** and has a Ki of 0.85 +/- 0.14 microM. 6-Thioorotate has a Ki of 82 +/- 8 microM which decreases to 3.8 +/- 1.4 microM in the presence of Zn2+. Zn2+ alone is a moderate **inhibitor** of **dihydroorotase** and does not enhance the potency of other **inhibitors**.(ABSTRACT TRUNCATED AT 250 WORDS)

L5 ANSWER 6 OF 78 MEDLINE on STN
ACCESSION NUMBER: 84114772 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6141293
TITLE: Design and synthesis of tetrahedral intermediate analogues as potential **dihydroorotase inhibitors**.
AUTHOR: Levenson C H; Meyer R B Jr
CONTRACT NUMBER: CA 30157 (NCI)
GM 29291 (NIGMS)
SOURCE: Journal of medicinal chemistry, **(1984 Feb)** 27 (2) 228-32.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198403
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840323
AB Three new heterocyclic analogues (4-6) of dihydroorotic acid were designed, synthesized, and tested as **inhibitors** of **dihydroorotase**. Each compound possessed a tetrahedral sulfur atom at the position equivalent to carbon 4 in the dihydroorotate ring in an attempt to mimic the presumed tetrahedral transition state in the course of the enzymatic reaction. Additionally, N-carbamyl-3-phosphonoalanine was prepared and evaluated as a **dihydroorotase inhibitor** . Compounds 4 and 6 were modest **inhibitors** (I50's of 0.52 and 0.18 mM, respectively), but the other candidate **inhibitors** showed little inhibition at 1 mM.

L5 ANSWER 7 OF 78 MEDLINE on STN
ACCESSION NUMBER: 91070538 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1979249
TITLE: Cytotoxic effects of **dihydroorotase inhibitors** upon human CCRF-CEM leukemia.
AUTHOR: Brooke J; Szabados E; Lyons S D; Goodridge R J; Harsanyi M C; Poiner A; Christopherson R I
CORPORATE SOURCE: Department of Biochemistry, University of Sydney, New South Wales, Australia.
SOURCE: Cancer research, **(1990 Dec 15)** 50 (24) 7793-8.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910308
Last Updated on STN: 19950206
Entered Medline: 19910123

AB 6-L-Thiodihydroorotate (TDHO) and 2-oxo-1,2,3,6-tetrahydropyrimidine-4,6-dicarboxylate (HDDP) are potent **inhibitors** of mammalian **dihydroorotase** in vitro (R. I. Christopherson, K. J. Schmalzl, E. Szabados, R. J. Goodridge, M. C. Harsanyi, M. E. Sant, E. M. Algar, J. E. Anderson, A. Armstrong, S. C. Sharma, W. A. Bubb, and S. D. Lyons, Biochemistry, 28: 463-470, 1989). Using human CCRF-CEM leukemia cells growing in culture, TDHO and HDDP as the free acids have 50% **inhibitory** concentration (IC50) values of 32 microM and greater than 1000 microM, respectively, whereas for TDHO methyl ester, the IC50 value is 25 microM, and for HDDP dimethyl ester, the IC50 value is 21 microM. These IC50 values were not affected by addition of dihydroorotate, uridine, or deoxycytidine to the culture medium. TDHO methyl ester (25 microM) had only slight **inhibitory** effects upon the **dihydroorotase** reaction of de novo pyrimidine biosynthesis in growing leukemia cells, cells arrested in G2 + M phases of the cell cycle. At 250 microM TDHO methyl ester, analysis of cell extracts by high-performance liquid chromatography showed that after 4 h carbamyl aspartate had accumulated from undetectable levels to 760 microM, whereas UTP decreased from 580 to 110 microM and CTP from 350 to 86 microM, indicating inhibition of **dihydroorotase** in growing leukemia cells. IMP accumulated from 63 to 350 microM, total guanylates increased while adenylates decreased, and the adenylate energy charge decreased from 0.91 to 0.69 after 4 h. The cellular concentration of 5-phosphoribosyl 1-pyrophosphate increased from 180 to 290 microM due to sparing from pyrimidine nucleotide biosynthesis resulting in complementary stimulation of the de novo purine pathway. HDDP dimethyl ester at concentrations of up to 250 microM had no discernable effect upon pyrimidine or purine nucleotide biosynthesis. At 25 microM HDDP-dimethyl ester, cells arrested in G2 + M phases initially, with accumulation of cells in G1/G0 at later times. These data suggest that the primary mechanisms of growth inhibition for TDHO and HDDP involve inhibition of cell cycle progression from late G2 or M phase to G1 phase and that blockade of the pyrimidine pathway by TDHO is a secondary effect found at higher concentrations.

L5 ANSWER 8 OF 78 MEDLINE on STN
ACCESSION NUMBER: 80159948 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6102565
TITLE: The effects of pH and **inhibitors** upon the catalytic activity of the **dihydroorotase** of multienzymatic protein pyr1-3 from mouse Ehrlich ascites carcinoma.
AUTHOR: Christopherson R I; Jones M E
SOURCE: Journal of biological chemistry, **(1980 Apr 25)** 255 (8) 3358-70.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198006
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 20000303
Entered Medline: 19800625

AB We have studied factors affecting the catalytic activity of **dihydroorotase** (EC 3.5.2.3), purified as part of a multienzymatic protein which contains carbamyl phosphate synthetase, aspartate transcarbamylase, and **dihydroorotase** (ME pyr1-3) and which initiates de novo pyrimidine biosynthesis in mouse Ehrlich ascites carcinoma. The apparent Km value for N-carbamyl-L-aspartate increases by 2 orders of magnitude as the pH increases from 7.0 to 8.3, consistent with

equilibration of **dihydroorotase** (E) between four states of protonation (E in equilibrium EH in equilibrium EH2 equilibrium EH3), where EH3 is the only catalytically active form of **dihydroorotase** for the biosynthetic reaction, having a Km for N-carbamyl-L-aspartate of 30 micro M. The apparent Km for L-dihydroorotate shows a converse dependence upon pH, remaining relatively constant at alkaline pH and increasing progressively as the pH is decreased below 7.0. These data are consistent with the above model if E and EH are catalytically active for the degradative reaction, both having Km values of 4.4 micro M for L-5,6-dihydroorotate. The D isomers of carbamylaspartate and dihydroorotate are also substrates for **dihydroorotase**. At pH 7.33, the apparent Km values for N-carbamyl-L-aspartate and N-carbamyl-D-aspartate are 247 and 204 micro M, respectively, but the Vmax for N-carbamyl-D-aspartate is only 1.7% of that obtained with N-carbamyl-L-aspartate. Orotate and a series of 5-substituted derivatives are competitive **inhibitors** of **dihydroorotase**. At pH 7.27, the apparent Ki for orotate using N-carbamyl-L-aspartate as substrate is 170 micro M and with L-5,6-dihydroorotate as substrate, the apparent Ki value is 9.6 micro M, suggesting that the enzyme exists in different forms in the presence of each substrate. **Dihydroorotase** is inhibited in a time-dependent manner by 50 mM L-cysteine and the presence of N-carbamyl-L-aspartate or L-5,6-dihydroorotate protects against this ultimately complete inactivation. 2-Mercaptoacetate, 2-mercaptoethylamine, 3-mercaptopropionate, and L-2,3-diaminopropionate have a similar although less potent **inhibitory** effect. To account for the data obtained, we propose a model for the equilibria existing between various protonated forms of **dihydroorotase** which is consistent with the pH dependencies of the apparent Km values observed and the Vmax values observed previously (Christopherson, R.I., and Jones, M.E. (1979) J. Biol. Chem. 254, 12506-12512). In addition, a catalytic mechanism is presented for the interconversion of N-carbamyl-L-aspartate and L-5,6-dihydroorotate.

L5 ANSWER 9 OF 78 MEDLINE on STN
ACCESSION NUMBER: 1999024036 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9804694
TITLE: Synthesis and enzymic evaluation of 4-mercapto-6-oxo-1, 4-azaphosphinane-2-carboxylic acid 4-oxide as an **inhibitor** of mammalian **dihydroorotase**.
AUTHOR: Manthey M K; Huang D T; Bubb W A; Christopherson R I
CORPORATE SOURCE: Department of Biochemistry, University of Sydney, Sydney, NSW 2006, Australia.
SOURCE: Journal of medicinal chemistry, **(1998 Nov 5)** 41 (23) 4550-5.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981130

AB The design, synthesis, and enzymic evaluation of cis- and trans-4-mercapto-6-oxo-1,4-azaphosphinane-2-carboxylic acid 4-oxide 5 against mammalian **dihydroorotase** is presented. The design strategy for 5 was based on the strong affinity of phosphinothioic acids for zinc and that 5 also resembles the postulated tetrahedral transition state for the enzyme-catalyzed reaction. The synthesis of 5 utilized a novel protection/deprotection sequence upon 4-hydroxy-6-oxo-1, 4-azaphosphinane-2-carboxylic acid 4-oxide 4, followed by incorporation of alpha-phenyl benzenemethanethiol and exhaustive deprotection to afford 5 in 40% overall yield from 4. The activities of both isomers of 5 as **inhibitors** of mammalian **dihydroorotase** were marginally greater than that of the parent phosphinic acid 4, indicating a weak

binding enhancement due to the phosphinothioic acid moiety.

L5 ANSWER 10 OF 78 MEDLINE on STN
ACCESSION NUMBER: 91107654 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1671037
TITLE: **Dihydroorotase** from Escherichia coli. Substitution of Co(II) for the active site Zn(II).
AUTHOR: Brown D C; Collins K D
CORPORATE SOURCE: Department of Biological Chemistry, University of Maryland Medical School, Baltimore 21201.
SOURCE: Journal of biological chemistry, **(1991 Jan 25)** 266 (3) 1597-604.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 19970203
Entered Medline: 19910227

AB Treatment of Escherichia coli **dihydroorotase** (a homodimer of subunit molecular weight 38,729) containing only the 1 active site Zn(II) ion per subunit with the sulfhydryl reagent N-(ethyl)-maleimide (NEM) blocks the two external Zn(II) sites per subunit and dramatically lessens the precipitation caused by high concentrations of Zn(II); stabilizes the enzyme partially against air oxidation and dilution inactivation; makes the active site Zn(II) easier to remove; and lowers Km and increases kcat. Treatment of NEM-blocked **dihydroorotase** ((NEM) **dihydroorotase**) with the chelator 2,6-pyridinedicarboxylic acid at pH 5.0 in the absence of oxygen and trace metal ions removes the active site Zn(II) with a half-life of 15 min, allowing the production of milligram amounts of moderately stable apo-(NEM)**dihydroorotase** in about 80% yield. Treatment of apo-(NEM)**dihydroorotase** with Co(II) at pH 7.0 produces (NEM)**dihydroorotase** completely substituted at the active site with Co(II) in 100% yield: analysis gives 0.95-1.1 g atoms of Co(II) per active site and 0.03-0.05 g atoms of Zn(II) per active site. This Co(II)-(NEM)**dihydroorotase** is hyperactive at pH 8. The electronic absorption spectrum of Co(II)-(NEM) **dihydroorotase** at pH 6.5 implicates an active site thiol group as a ligand to the metal ion. The spectrum is inconsistent with tetrahedral coordination of the active site metal ion and is most consistent with a pentacoordinate structure.

=> d l5 11-20

L5 ANSWER 11 OF 78 MEDLINE on STN
AN 90133790 MEDLINE
DN PubMed ID: 1967653
TI Analogues of carbamyl aspartate as **inhibitors** of **dihydroorotase**: preparation of boronic acid transition-state analogues and a zinc chelator carbamylhomocysteine.
AU Kinder D H; Frank S K; Ames M M
CS Department of Oncology, Mayo Clinic & Foundation, Rochester, Minnesota 55905.
NC CA 15083 (NCI)
SO Journal of medicinal chemistry, **(1990 Feb)** 33 (2) 819-23.
Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199003
ED Entered STN: 19900328

Last Updated on STN: 19970203
Entered Medline: 19900309

L5 ANSWER 12 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:795993 HCAPLUS
DN 132:31743
TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Limited, UK
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9964626 | A2 | 19991216 | WO 1999-GB1779 | 19990604 <-- |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2330929 | AA | 19991216 | CA 1999-2330929 | 19990604 <-- |
| | AU 9941586 | A1 | 19991230 | AU 1999-41586 | 19990604 <-- |
| | AU 766544 | B2 | 20031016 | | |
| | AU 9941587 | A1 | 19991230 | AU 1999-41587 | 19990604 <-- |
| | GB 2339200 | A1 | 20000119 | GB 1999-12914 | 19990604 |
| | GB 2339200 | B2 | 20010912 | | |
| | EP 1084273 | A1 | 20010321 | EP 1999-925207 | 19990604 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2003528564 | T2 | 20030930 | JP 2000-553616 | 19990604 |
| | US 2003198970 | A1 | 20031023 | US 2002-206568 | 20020729 |
| PRAI | GB 1998-12098 | A | 19980606 | | |
| | GB 1998-28289 | A | 19981223 | | |
| | GB 1998-16086 | A | 19980724 | | |
| | GB 1998-16921 | A | 19980805 | | |
| | GB 1998-17097 | A | 19980807 | | |
| | GB 1998-17200 | A | 19980808 | | |
| | GB 1998-17632 | A | 19980814 | | |
| | GB 1998-17943 | A | 19980819 | | |
| | US 1999-325123 | B1 | 19990603 | | |
| | WO 1999-GB1779 | W | 19990604 | | |

L5 ANSWER 13 OF 78 MEDLINE on STN
AN 96009619 MEDLINE
DN PubMed ID: 7547862
TI Catalysis by hamster **dihydroorotase**: zinc binding, site-directed mutagenesis, and interaction with **inhibitors**.
AU Williams N K; Manthey M K; Hambley T W; O'Donoghue S I; Keegan M; Chapman B E; Christopherson R I
CS Department of Biochemistry, University of Sydney, Australia.
SO Biochemistry, **(1995 Sep 12)** 34 (36) 11344-52.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199510
ED Entered STN: 19951227

Last Updated on STN: 19970203
Entered Medline: 19951025

L5 ANSWER 14 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:795994 HCAPLUS
DN 132:31744
TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Ltd., UK
SO PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9964627 | A2 | 19991216 | WO 1999-GB1780 | 19990604 <-- |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | |
|---|---|---|---|
| PRAI | GB 1998-12099 | A | 19980606 |
| | GB 1998-13291 | A | 19980620 |
| | GB 1998-13611 | A | 19980624 |
| | GB 1998-13835 | A | 19980627 |
| | GB 1998-14110 | A | 19980701 |
| | GB 1998-14580 | A | 19980707 |
| | GB 1998-15438 | A | 19980716 |
| | GB 1998-15574 | A | 19980718 |
| | GB 1998-15576 | A | 19980718 |
| | GB 1998-16085 | A | 19980724 |
| | GB 1998-16086 | A | 19980724 |
| | GB 1998-16921 | A | 19980805 |
| | GB 1998-17097 | A | 19980807 |
| | GB 1998-17200 | A | 19980808 |
| | GB 1998-17632 | A | 19980814 |
| | GB 1998-17943 | A | 19980819 |

L5 ANSWER 15 OF 78 MEDLINE on STN
AN 88259140 MEDLINE
DN PubMed ID: 2898532
TI cis-4-Carboxy-6-(mercaptomethyl)-3,4,5,6-tetrahydropyrimidin-2(1 H)-one , a potent **inhibitor** of mammalian **dihydroorotase**.
AU Adams J L; Meek T D; Mong S M; Johnson R K; Metcalf B W
CS Department of Medicinal Chemistry, Smith Kline & French Laboratories, Swedeland, Pennsylvania 19479.
SO Journal of medicinal chemistry, **(1988 Jul)** 31 (7) 1355-9.
Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198808
ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880805

L5 ANSWER 16 OF 78 MEDLINE on STN
AN 81069802 MEDLINE

DN PubMed ID: 6108323
TI The overall synthesis of L-5,6-dihydroorotate by multienzymatic protein pyr1-3 from hamster cells. Kinetic studies, substrate channeling, and the effects of **inhibitors**.
AU Christopherson R I; Jones M E
NC HD12787 (NICHD)
P30-CA16086 (NCI)
SO Journal of biological chemistry, **(1980 Dec 10)** 255 (23) 11381-95.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198102
ED Entered STN: 19900316
Last Updated on STN: 19980206
Entered Medline: 19810219

L5 ANSWER 17 OF 78 MEDLINE on STN
AN 96106132 MEDLINE
DN PubMed ID: 8572888
TI Purification and characterization of **dihydroorotase** from Pseudomonas putida.
AU Ogawa J; Shimizu S
CS Department of Agricultural Chemistry, Kyoto University, Japan.
SO Archives of microbiology, **(1995 Nov)** 164 (5) 353-7.
Journal code: 0410427. ISSN: 0302-8933.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199603
ED Entered STN: 19960315
Last Updated on STN: 19970203
Entered Medline: 19960305

L5 ANSWER 18 OF 78 MEDLINE on STN
AN 92222463 MEDLINE
DN PubMed ID: 1348618
TI Antimalarial activity of orotate analogs that inhibit **dihydroorotase** and dihydroorotate dehydrogenase.
AU Krungkrai J; Krungkrai S R; Phakanont K
CS Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
SO Biochemical pharmacology, **(1992 Mar 17)** 43 (6) 1295-301.
Journal code: 0101032. ISSN: 0006-2952.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199205
ED Entered STN: 19920529
Last Updated on STN: 19970203
Entered Medline: 19920513

L5 ANSWER 19 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN
AN 93:284937 SCISEARCH
GA The Genuine Article (R) Number: KZ974
TI EXPRESSION OF CATALYTICALLY ACTIVE HAMSTER **DIHYDROOROTASE** DOMAIN IN ESCHERICHIA-COLI - PURIFICATION AND CHARACTERIZATION
AU WILLIAMS N K; YIN P D; SEYMOUR K K; RALSTON G B; CHRISTOPHERSON R I (Reprint)
CS UNIV SYDNEY, DEPT BIOCHEM, SYDNEY, NSW 2006, AUSTRALIA

CYA AUSTRALIA
SO PROTEIN ENGINEERING, (**APR 1993**) Vol. 6, No. 3, pp. 333-340.
ISSN: 0269-2139.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 24
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

L5 ANSWER 20 OF 78 MEDLINE on STN
AN 86102131 MEDLINE
DN PubMed ID: 2867744
TI Enzyme elements involved in the interconversion of L-carbamylaspartate and L-dihydroorotate by **dihydroorotase** from Clostridium oroticum.
AU Pettigrew D W; Mehta B J; Bidigare R R; Choudhury R R; Scheffler J E; Sander E G
NC CA29568 (NCI)
GM30911 (NIGMS)
SO Archives of biochemistry and biophysics, (**1985 Dec**) 243 (2) 447-53.
Journal code: 0372430. ISSN: 0003-9861.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198601
ED Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860130

=> d l5 21-30

L5 ANSWER 21 OF 78 MEDLINE on STN
AN 82110511 MEDLINE
DN PubMed ID: 6119898
TI Chemotherapeutic **inhibitors** of the enzymes of the de novo pyrimidine pathway.
AU Kensler T W; Cooney D A
SO Advances in pharmacology and chemotherapy, (**1981**) 18 273-352.
Ref: 197
Journal code: 0237113. ISSN: 0065-3144.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 198203
ED Entered STN: 19900317
Last Updated on STN: 19980206
Entered Medline: 19820313

L5 ANSWER 22 OF 78 MEDLINE on STN
AN 95284036 MEDLINE
DN PubMed ID: 7766613
TI Function of conserved histidine residues in mammalian **dihydroorotase**.
AU Zimmermann B H; Kemling N M; Evans D R
CS Department of Biochemistry, University of Puerto Rico, San Juan 00936-5067.
NC GM47399 (NIGMS)
RR-03051 (NCRR)
SO Biochemistry, (**1995 May 30**) 34 (21) 7038-46.
Journal code: 0370623. ISSN: 0006-2960.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507
ED Entered STN: 19950713
Last Updated on STN: 19970203
Entered Medline: 19950703

L5 ANSWER 23 OF 78 MEDLINE on STN
AN 94227059 MEDLINE
DN PubMed ID: 7909690
TI Cytotoxic effects of **inhibitors** of de novo pyrimidine biosynthesis upon Plasmodium falciparum.
AU Seymour K K; Lyons S D; Phillips L; Rieckmann K H; Christopherson R I
CS Department of Biochemistry, University of Sydney, New South Wales, Australia.
SO Biochemistry, **(1994 May 3)** 33 (17) 5268-74.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940620
Last Updated on STN: 19970203
Entered Medline: 19940608

L5 ANSWER 24 OF 78 MEDLINE on STN
AN 83241362 MEDLINE
DN PubMed ID: 6134826
TI Enzymes of de novo pyrimidine biosynthesis in Babesia rodhaini.
AU Holland J W; Gero A M; O'Sullivan W J
SO Journal of protozoology, **(1983 Feb)** 30 (1) 36-40.
Journal code: 2985197R. ISSN: 0022-3921.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198308
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19830826

L5 ANSWER 25 OF 78 MEDLINE on STN
AN 82007717 MEDLINE
DN PubMed ID: 6115855
TI Phosphorylation and dephosphorylation of carbamoyl-phosphate synthetase II complex of rat ascites hepatoma cells.
AU Otsuki T; Mori M; Tatibana M
SO Journal of biochemistry, **(1981 May)** 89 (5) 1367-74.
Journal code: 0376600. ISSN: 0021-924X.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198111
ED Entered STN: 19900316
Last Updated on STN: 19980206
Entered Medline: 19811118

L5 ANSWER 26 OF 78 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
AN 1998:331650 BIOSIS
DN PREV199800331650
TI Looking for **dihydroorotase inhibitors** using phage

display.
AU Robles Lopez, S. M.; Zimmermann, B. H.
CS Univ. Puerto Rico, San Juan, Puerto Rico
SO FASEB Journal, (April 24, 1998) Vol. 12, No. 8, pp. A1444. print.
Meeting Info.: Meeting of the American Society for Biochemistry and Molecular Biology. Washington, D.C., USA. May 16-20, 1998. American Society for Biochemistry and Molecular Biology.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 12 Aug 1998
Last Updated on STN: 12 Aug 1998

L5 ANSWER 27 OF 78 MEDLINE on STN
AN 96227151 MEDLINE
DN PubMed ID: 8654860
TI **Inhibitors** of dihydro-orotase, amidophosphoribosyltransferase and IMP cyclohydrolase as potential drugs.
AU Christopherson R I; Williams N K; Schoettle S L; Szabados E; Hambley T W; Manthey M K
CS Department of Biochemistry, University of Sydney, NSW, Australia.
SO Biochemical Society transactions, **(1995 Nov)** 23 (4) 888-93.
Journal code: 7506897. ISSN: 0300-5127.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199607
ED Entered STN: 19960808
Last Updated on STN: 19960808
Entered Medline: 19960730

L5 ANSWER 28 OF 78 MEDLINE on STN
AN 96020160 MEDLINE
DN PubMed ID: 8590465
TI As in Saccharomyces cerevisiae, aspartate transcarbamoylase is assembled on a multifunctional protein including a **dihydroorotase**-like cryptic domain in Schizosaccharomyces pombe.
AU Lollier M; Jaquet L; Nedeva T; Lacroute F; Potier S; Souciet J L
CS Laboratoire de Microbiologie et de Genetique, URA n-1481 Universite Louis-Pasteur/CNRS, Strasbourg, France.
SO Current genetics, **(1995 Jul)** 28 (2) 138-49.
Journal code: 8004904. ISSN: 0172-8083.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M27174; GENBANK-X81841; SWISSPROT-P08955; SWISSPROT-P20054
EM 199603
ED Entered STN: 19960404
Last Updated on STN: 19980206
Entered Medline: 19960328

L5 ANSWER 29 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:672661 HCAPLUS
DN 115:272661
TI Recombinant Escherichia coli for the manufacture of pyrimidine deoxyribonucleosides
IN McDandliss, Russell J.; Anderson, David M.
PA ChemGen Corp., USA
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9109130 | A1 | 19910627 | WO 1990-US6993 | 19901205 <-- |
| | W: AU, CA, JP, KR | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| | US 5213972 | A | 19930525 | US 1989-448158 | 19891208 <-- |
| | CA 2070826 | AA | 19910609 | CA 1990-2070826 | 19901205 <-- |
| | CA 2070826 | C | 20011030 | | |
| | AU 9170374 | A1 | 19910718 | AU 1991-70374 | 19901205 <-- |
| | AU 642199 | B2 | 19931014 | | |
| | EP 504279 | A1 | 19920923 | EP 1991-901364 | 19901205 <-- |
| | EP 504279 | B1 | 19970709 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | AT 155170 | E | 19970715 | AT 1991-901364 | 19901205 <-- |
| | ES 2107451 | T3 | 19971201 | ES 1991-901364 | 19901205 <-- |
| | JP 3032292 | B2 | 20000410 | JP 1990-501749 | 19901205 |
| | JP 05504055 | T2 | 19930701 | JP 1991-501749 | 19911223 <-- |
| | JP 3032292 | B2 | 20000410 | | |
| PRAI | US 1989-448158 | A | 19891208 | | |
| | WO 1990-US6993 | A | 19901205 | | |

L5 ANSWER 30 OF 78 MEDLINE on STN
AN 96227309 MEDLINE
DN PubMed ID: 8654805
TI Identification of the binding site for the allosteric inactivator UTP in mammalian CPS II.
AU Zhu L M; Carrey E A
CS Department of Biochemistry, University of Dundee.
SO Biochemical Society transactions, **(1995 Nov)** 23 (4) 620S.
Journal code: 7506897. ISSN: 0300-5127.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199607
ED Entered STN: 19960808
Last Updated on STN: 19980206
Entered Medline: 19960730

=> d l5 24 ab

L5 ANSWER 24 OF 78 MEDLINE on STN
AB The pathway of de novo pyrimidine biosynthesis in the rodent parasitic protozoa Babesia rodhaini has been investigated. Specific activities of five of the six enzymes of the pathway were determined: aspartate transcarbamylase (ATCase: E.C. 2.1.3.2); **dihydroorotase** (DHOase: E.C. 3.5.2.3); dihydroorotate dehydrogenase (DHO-DHase: E.C. 1.3.3.1); orotate phosphoribosyltransferase (OPRTase: E.C. 2.4.2.10); and orotidine-5'-phosphate decarboxylase (ODCase: E.C. 4.1.1.23). Michaelis constants for ATCase, DHO-DHase, OPRTase, and ODCase were determined in whole homogenates. Several substrate analogs were also investigated as **inhibitors** and **inhibitor** constants determined.
N-(phosphonacetyl)-L-aspartate was shown to be an **inhibitor** of the ATCase with an apparent Ki of 7 microM. Dihydro-5-azaorotate inhibited the DHO-DHase (Ki, 16 microM) and 5-azaorotate (Ki, 21 microM) was an **inhibitor** of the OPRTase. The UMP analog, 6-aza-UMP (Ki, 0.3 microM) was a potent **inhibitor** of ODCase, while lower levels of inhibition were found with the product, UMP (Ki, 120 microM) and the purine nucleotide, XMP (Ki, 95 microM). Additionally, menoctone, a ubiquinone analog, was shown to inhibit DHO-DHase.

=> d l5 31-40

L5 ANSWER 31 OF 78 MEDLINE on STN
AN 92031468 MEDLINE
DN PubMed ID: 1681900
TI Identification of the ATP binding sites of the carbamyl phosphate synthetase domain of the Syrian hamster multifunctional protein CAD by affinity labeling with 5'-[p-(fluorosulfonyl)benzoyl]adenosine.
AU Kim H S; Lee L; Evans D R
CS Department of Biochemistry, Wayne State University School of Medicine, Detroit, Michigan 48201.
NC CA27674 (NCI)
SO Biochemistry, **(1991 Oct 22)** 30 (42) 10322-9.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199111
ED Entered STN: 19920124
Last Updated on STN: 20020420
Entered Medline: 19911125

L5 ANSWER 32 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:644516 HCAPLUS
DN 127:307358
TI Synthesis and exchange reactions of 5-alkyl-2-oxo-6-thioxo-1,2,3,6-hexahydropyrimidine-4-carboxylic acids
AU Batty, Craig A.; Manthey, Michael K.; Kirk, Julie; Manthey, Monika; Christopherson, Richard I.; Hambley, Trevor
CS Department of Biochemistry, University of Sydney, Sydney, NSW 2006, Australia
SO Journal of Heterocyclic Chemistry (**1997**), 34(4), 1355-1367
CODEN: JHTCAD; ISSN: 0022-152X
PB HeteroCorporation
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1982:194351 HCAPLUS
DN 96:194351
TI Analysis of CAD gene amplification using molecular cloning, gene transfer, and cytogenetics
AU Wahl, Geoffrey M.; Allen, Virginia; Delbrueck, Suzanne; Eckhart, Walter; Meinkoth, Judy; Padgett, Rick; De Saint Vincent, Bruno Robert; Rubnitz, Jeffrey; Stark, George; Vitto, Louise
CS Tumor Virol. Lab., Salk Inst. Biol. Stud., La Jolla, CA, 92037, USA
SO Gene Amplif. [Conf.] (**1982**), Meeting Date 1981, 167-75.
Editor(s): Schimke, Robert T. Publisher: Cold Spring Harbor Lab., Cold Spring Harbor, N. Y.
CODEN: 47NNA3
DT Conference
LA English

L5 ANSWER 34 OF 78 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
AN 1987:370609 BIOSIS
DN PREV198733061084; BR33:61084
TI PREPARATION OF BORON AND SULFUR CONTAINING ACTIVE SITE DIRECTED **INHIBITORS** OF **DIHYDROOROTASE** DHO.
AU KINDER D H [Reprint author]; FRANK S K; AMES M M
CS DEP ONCOL, MAYO CLINIC AND FOUND, ROCHESTER, MINN 55905, USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1987) Vol. 28, pp. 329.

Meeting Info.: SEVENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, ATLANTA, GEORGIA, USA, MAY 20-23, 1987. PROC AM ASSOC CANCER RES ANNU MEET.
ISSN: 0197-016X.
DT Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 29 Aug 1987
Last Updated on STN: 29 Aug 1987

L5 ANSWER 35 OF 78 MEDLINE on STN
AN 95257934 MEDLINE
DN PubMed ID: 7739536
TI An E-box-mediated increase in cad transcription at the G1/S-phase boundary is suppressed by **inhibitory** c-Myc mutants.
AU Miltenberger R J; Sukow K A; Farnham P J
CS McArdle Laboratory for Cancer Research, University of Wisconsin-Madison Medical School 53706, USA.
NC CA07175 (NCI)
CA09135 (NCI)
CA59524 (NCI)
SO Molecular and cellular biology, **(1995 May)** 15 (5) 2527-35.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 19950615
Last Updated on STN: 19980206
Entered Medline: 19950602

L5 ANSWER 36 OF 78 MEDLINE on STN
AN 93156739 MEDLINE
DN PubMed ID: 7679200
TI DNA topoisomerase II inhibition and gene amplification in V79/B7 cells.
AU Di Leonardo A; Cavolina P; Maddalena A
CS Dipartimento di Biologia Cellulare e dello Sviluppo, A. Monroy, University of Palermo, Italy.
SO Mutation research, **(1993 Mar)** 301 (3) 177-82.
Journal code: 0400763. ISSN: 0027-5107.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199303
ED Entered STN: 19930326
Last Updated on STN: 19980206
Entered Medline: 19930309

L5 ANSWER 37 OF 78 MEDLINE on STN
AN 86164666 MEDLINE
DN PubMed ID: 2869965
TI Overproduction of the first three enzymes of pyrimidine nucleotide biosynthesis in Drosophila cells resistant to N-phosphonacetyl-L-aspartate.
AU Laval M; Azou Y; Giorgi D; Rosset R
SO Experimental cell research, **(1986 Apr)** 163 (2) 381-95.
Journal code: 0373226. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198605
ED Entered STN: 19900321

Last Updated on STN: 19980206
Entered Medline: 19860501

L5 ANSWER 38 OF 78 MEDLINE on STN
AN 83219079 MEDLINE
DN PubMed ID: 6855812
TI Enzymes of the de novo pyrimidine biosynthetic pathway in Toxoplasma gondii.
AU Asai T; O'Sullivan W J; Kobayashi M; Gero A M; Yokogawa M; Tatibana M
SO Molecular and biochemical parasitology, **(1983 Feb)** 7 (2) 89-100.
Journal code: 8006324. ISSN: 0166-6851.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198307
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19830715

L5 ANSWER 39 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN
AN 1999:984275 SCISEARCH
GA The Genuine Article (R) Number: 260QN
TI Looking for **dihydroorotase inhibitors** using phage display
AU Lopez S M R (Reprint); Zimmermann B H
CS UNIV PUERTO RICO, SAN JUAN, PR 00936
CYA USA
SO FASEB JOURNAL, (**24 APR 1998**) Vol. 12, No. 8, Supp. [S], pp. 771-771.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0892-6638.
DT Conference; Journal
FS LIFE
LA English
REC Reference Count: 0

L5 ANSWER 40 OF 78 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN
AN 96:589008 SCISEARCH
GA The Genuine Article (R) Number: VA593
TI ASSAY OF ESCHERICHIA-COLI **DIHYDROOROTASE** WITH ENANTIOMERIC SUBSTRATE - PRACTICAL PREPARATION OF CARBAMYL L-ASPARTATE AND HIGH-PERFORMANCE LIQUID-CHROMATOGRAPHY ANALYSIS OF CATALYSIS PRODUCT
AU DANIEL R (Reprint); KOKEL B; CAMINADE E; MARTEL A; LEGOFFIC F
CS UNIV PARIS 13, LAB RECH MACROMOL, URA 502 CNRS, AVE JB CLEMENT, F-93430 VILLETANEUSE, FRANCE (Reprint); ECOLE NATL SUPER CHIM, CNRS, LAB BIOORGAN & BIOTECHNOL, F-75231 PARIS 05, FRANCE
CYA FRANCE
SO ANALYTICAL BIOCHEMISTRY, (**01 AUG 1996**) Vol. 239, No. 2, pp. 130-135.
ISSN: 0003-2697.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 13
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

=> d l5 32 ab

L5 ANSWER 32 OF 78 HCAPLUS COPYRIGHT 2005 ACS on STN
AB An improved prepn. of 2-oxo-6-thioxo-1,2,3,6-hexahydropyrimidine-4-

carboxylic acid (I), a potent **inhibitor** of **dihydroorotase** is presented. Trans-5-alkyl-2-oxo-6-thioxohexahydropyrimidine-4-carboxylic acids II (R = Me, Et, n-Pr) were synthesized via the thiation of the p-methoxybenzyl esters of 5-alkyldihydroorotic acids with Lawesson's reagent followed by subsequent de-protection. The corresponding cis isomers were prepd. by redn. of 5-alkyl-6-thioxoorotic acids with zinc in acetic acid. The stability and exchange reactions of II under physiol. conditions were investigated by UV and 1H NMR spectroscopy. The attempted synthesis of diazabicyclononanecarboxylic acid III, a fused cyclopentyl deriv. of I is also presented.

=> d his

(FILE 'HOME' ENTERED AT 11:24:00 ON 16 FEB 2005)

FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT 11:25:02 ON 16 FEB 2005
L1 273 S INHIBITOR? AND DIHYDROOROTASE
L2 146 DUP REM L1 (127 DUPLICATES REMOVED)
L3 3 S L2 AND (PLANT? OR SOLANUM OR ARBIDOPSIS OR TOBACCO OR WHEAT)
L4 78 S L2 AND 1980-1999/PY
L5 78 FOCUS L4 1-

=> s l4 and plant
L6 1 L4 AND PLANT

=> d l6 ibib ab

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:748948 HCAPLUS
DOCUMENT NUMBER: 128:150233
TITLE: The complete genome sequence of the gram-positive bacterium Bacillus subtilis
AUTHOR(S): Kunst, F.; Ogasawara, N.; Moszer, I.; Albertini, A. M.; Alloni, G.; Azevedo, V.; Bertero, M. G.; Bessieres, P.; Bolotin, A.; Borchert, S.; Borriss, R.; Boursier, L.; Brans, A.; Braun, M.; Brignell, S. C.; Bron, S.; Brouillet, S.; Bruschi, C. V.; Caldwell, B.; Capuano, V.; Carter, N. M.; Choi, S.-K.; Codani, J.-J.; Connerton, I. F.; Cummings, N. J.; Daniel, R. A.; Denizot, F.; Devine, K. M.; Dusterhoft, A.; Ehrlich, S. D.; Emmerson, P. T.; Entian, K. D.; Errington, J.; Fabret, C.; Ferrari, E.; Foulger, D.; Fritz, C.; Fujita, M.; Fujita, Y.; Fuma, S.; Galizzi, A.; Galleron, N.; Ghim, S.-Y.; Glaser, P.; Goffeau, A.; Golightly, E. J.; Grandi, G.; Guiseppi, G.; Guy, B. J.; Haga, K.; et al.
CORPORATE SOURCE: Unite de Biochemie Microbienne, Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Nature (London) (**1997**), 390(6657), 249-256
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacillus subtilis is the best-characterized member of the gram-pos. bacteria. Its genome of 4,214,810 base pairs comprises 4100 protein-coding genes. Of these protein-coding genes, 53% are represented once, while a quarter of the genome corresponds to several gene families that have been greatly expanded by gene duplication, the largest family contg. 77 putative ATP-binding transport proteins. In addn., a large proportion of the genetic capacity is devoted to the utilization of a variety of carbon sources, including many **plant**-derived mols. The identification of 5 signal peptidase genes, as well as several genes

for components of the secretion app., is important given the capacity of Bacillus strains to secrete large amts. of industrially important enzymes. Many of the genes are involved in the synthesis of secondary metabolites, including antibiotics, that are more typically assocd. with Streptomyces species. The genome contains .gtoreq.10 prophages or remnants of prophages, indicating that bacteriophage infection has played an important evolutionary role in horizontal gene transfer, in particular in the propagation of bacterial pathogenesis.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s plant hydroorotase
L7 0 PLANT HYDROOROTASE

=> s plant dihydroorotase
L8 1 PLANT DIHYDROOROTASE

=> d l8 ibib ab

L8 ANSWER 1 OF 1 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2001-08527 BIOTECHDS
TITLE: New DNA encoding **plant dihydroorotase**, for producing herbicide-resistant plants and for screening for compounds that can inhibit dihydroorotase and that can be used as herbicides;
tobacco and Arabidopsis thaliana transgenic plant construction
AUTHOR: Ehrhardt T; Lerchl J; Stitt N M; Zrenner R; Schroeder M
PATENT ASSIGNEE: BASF
LOCATION: Ludwigshafen, Germany.
PATENT INFO: WO 2001018190 15 Mar 2001
APPLICATION INFO: WO 2000-EP8581 2 Sep 2000
PRIORITY INFO: DE 1999-1042742 7 Sep 1999
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 2001-235198 [24]
AB A DNA sequence (I) containing the coding region for a **plant dihydroorotase** (DHO, EC-3.5.2.3) with a DNA sequence (S1) of 1,271 bp is claimed. Also claimed are: a DNA sequence that hybridizes to (S1) and encodes a protein with DHO activity; a protein containing 100 amino acids from a 346 residue protein sequence; identifying substances that inhibit activity of DHO or act as herbicides by inhibition of DHO; and a test system based on expression of (S1) for identifying herbicidal inhibitors of DHA. In an example, a cDNA bank from potato was constructed in plasmid pBS-SK and tested in for complementation of the defect in Escherichia coli CGSC5152 which lacks the DHO gene. The longest clone was sequenced (S1) which included a 1,049 bp open reading frame that encodes DHO. The gene was expressed in vector/host system as a fusion protein or introduced into plant transformation vectors. A sequence of 1,962 bp was isolated from tobacco (Nicotiana tabacum) cDNA bank by using a DNA probes encoding DHO in Arabidopsis thaliana. The above can be used to produce DHO and to produce plants with increased resistance to DHO-inactivating herbicides. (38pp)

=> d his

(FILE 'HOME' ENTERED AT 11:24:00 ON 16 FEB 2005)

FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT 11:25:02 ON 16 FEB 2005
L1 273 S INHIBITOR? AND DIHYDROOROTASE
L2 146 DUP REM L1 (127 DUPLICATES REMOVED)
L3 3 S L2 AND (PLANT? OR SOLANUM OR ARBIDOPSIS OR TOBACCO OR WHEAT)

```
L4            78 S L2 AND 1980-1999/PY
L5            78 FOCUS L4 1-
L6             1 S L4 AND PLANT
L7             0 S PLANT HYDROOROTASE
L8             1 S PLANT DIHYDROOROTASE

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                  101.80     102.22

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -5.84      -5.84

STN INTERNATIONAL LOGOFF AT 11:45:20 ON 16 FEB 2005
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=> d l2 1-3 ibib ab

L2 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 2003114535 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12626710
TITLE: Dihydropyrimidine amidohydrolases and dihydroorotases share the same origin and several enzymatic properties.
AUTHOR: Gojkovic Zoran; Rislund Lise; Andersen Birgit; Sandrini Michael P B; Cook Paul F; Schnackerz Klaus D; Piskur Jure
CORPORATE SOURCE: Eukaryote Molecular Biology, BioCentrum-DTU, Technical University of Denmark, Building 301, DK-2800 Lyngby, Denmark.
SOURCE: Nucleic acids research, (2003 Mar 15) 31 (6) 1683-92. Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030312
Last Updated on STN: 20030331
Entered Medline: 20030328

AB Slime mold, plant and insect dihydropyrimidine amidohydrolases (DHPases, EC 3.5.2.2), which catalyze the second step of pyrimidine and several anti-cancer drug degradations, were cloned and shown to functionally replace a defective DHPase enzyme in the yeast Saccharomyces kluyveri. The yeast and slime mold DHPases were over-expressed, shown to contain two zinc ions, characterized for their properties and compared to those of the calf liver enzyme. In general, the kinetic parameters varied widely among the enzymes, the mammalian DHPase having the highest catalytic efficiency. The ring opening was catalyzed most efficiently at pH 8.0 and competitively inhibited by the reaction product, N-carbamyl-beta-alanine. At lower pH values DHPases catalyzed the reverse reaction, the closing of the ring. Apparently, eukaryote DHPases are enzymatically as well as phylogenetically related to the de novo biosynthetic **dihydroorotase** (DHOase) enzymes. Modeling studies showed that the position of the catalytically critical amino acid residues of bacterial DHOases and eukaryote DHPases overlap. Therefore, only a few modifications might have been necessary during evolution to convert the unspecialized enzyme into anabolic and catabolic ones.

L2 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:504932 HCAPLUS
DOCUMENT NUMBER: 137:74413
TITLE: Transgenic plants expressing sugar beet genes involved in stress tolerance and their uses for salt stress resistance
INVENTOR(S): Kanhonou, Rodolphe Arthur; Serrano Salom, Ramon; Ros Palau, Roque
PATENT ASSIGNEE(S): Cropdesign N.V., Belg.
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002052012 | A2 | 20020704 | WO 2001-EP15093 | 20011220 |
| WO 2002052012 | C1 | 20030220 | | |
| WO 2002052012 | A3 | 20020912 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| CA 2432380 | AA | 20020704 | CA 2001-2432380 | 20011220 |
| EP 1343875 | A2 | 20030917 | EP 2001-986428 | 20011220 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

| | | | | |
|---|---|---|---|---|
| JP 2004524015 | T2 | 20040812 | JP 2002-553492 | 20011220 |
| US 2004111769 | A1 | 20040610 | US 2004-451554 | 20040126 |
| PRIORITY APPLN. INFO.: | | | EP 2000-870319 A | 20001222 |
| | | | US 2001-271656P P | 20010226 |
| | | | WO 2001-EP15093 W | 20011220 |

AB The present invention relates to isolated genes originating from Beta vulgaris, sugar beet, that are involved in responses to stress situations. The genes were isolated from a sugar beet cDNA library screened in a functional selection procedure with transformed yeast cells that were able to grow in selection medium with high salt concns. Subsequently these genes were sequenced and further characterized. One of the genes is a sugar beet casein kinase .alpha.-subunit (BvCK2A), one is a sugar beet **dihydroorotase** (BvDHO), one is a sugar beet translation initiation factor 1A (BvelF-1A) and two others are of a unknown protein type (Bv120 and Bv20Li). The expression level of BvCK2A gene was enhanced under salt stress condition and the transgenic rice and **Arabidopsis** expressing BvCK2A exhibited resistance to salt. All of these isolated plant genes were functional as stress tolerance enhancers in yeast cells and are therefore useful to confer stress tolerance to an organism when transfected herein. More particularly, these genes can be used to render crops resistant to stress situations like osmotic stress caused by salt, drought, cold or frost.

L2 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2001:152854 HCAPLUS |
| DOCUMENT NUMBER: | 134:205156 |
| TITLE: | Transgenic plants with increased polysaccharide content overexpressing **dihydroorotase** |
| INVENTOR(S): | Ehrhardt, Thomas; Stitt Nigel, Marc; Geigenberger, Peter Ludwig; Loef, Irene; Zrenner, Rita; Schroeder, Michael |
| PATENT ASSIGNEE(S): | BASF A.-G., Germany |
| SOURCE: | PCT Int. Appl., 32 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | German |
| FAMILY ACC. NUM. COUNT: | 1 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001014569 | A2 | 20010301 | WO 2000-EP7884 | 20000812 |
| WO 2001014569 | A3 | 20011011 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | DE 1999-19939688 | A | 19990820 |

AB The invention relates to a method of producing plants with an increased polysaccharide content that are obtained by overexpressing a gene of the

pyrimidine metab. such as **dihydroorotase**. Thus, potato, tobacco, and **Arabidopsis** thaliana expressing, from the 35S promoter, a chimeric gene encoding tobacco transketolase transit peptide fused to potato **dihydroorotase** were prepd. These transgenic plants exhibited increased levels of uridine nucleotides and starch.

=> log y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 11.88 | 12.09 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -1.46 | -1.46 |

STN INTERNATIONAL LOGOFF AT 11:50:18 ON 16 FEB 2005